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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,609	10/13/2000	Roberto Weinmann	BMS-0010	9813

7590 10/28/2003

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

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DATE MAILED: 10/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/687,609

Applicant(s)

WEINMANN ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 11 and 13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 11 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

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DETAILED ACTION

Applicants' arguments, filed 23 July 2003, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

The Supplemental IDS, filed 4 February 2003 has been entered and considered, as per Applicant's request an initialed copy of the form PTO-1449 is included with this office action.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1 recite "AR-LBD" without defining it for a first time. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 11, and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to obtain a crystal of AR-LBD complexed with AR-LBD ligand. For the reasons discussed below, this constitutes undue experimentation.

b) and d) The specification provides the three-dimensional structure of the AR-LBD/dihydroxytestosterone complex in Table A and describes the crystallization conditions for this particular complex at pages 27-28. The specification does not provide guidance on crystallization of any other AR-LBD with any or all ligands, as encompassed by the instant claims. In fact, the specification states that ligands that interact with the AR can be agonists, antagonists, etc. that would all cause different conformational changes (page 18, beginning line 7). Furthermore, with the different ligands contemplated on page 6 (any peptide, peptide mimetic, any nonpeptide, small organic molecule) one of skill in the art would not reasonably expect to successfully use the same crystallization conditions for the variety of different ligands listed. There are no other examples in the specification. Without similar guidance for the specific generation of AR-LBD complexed with **any** ligand other than dihydroxytestosterone

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attempting to form a crystal of AR-LBD complexed with any ligand other than DHT would represent undue experimentation. Therefore, the present invention is not enabled.

c) The specification provides only working examples of AR-LBD/dihydroxytestosterone complex.

e) and g) It would have been well known in the art that crystallization techniques are complex. It is well established that the utilization of a variety of crystallization methods, for any protein in question, greatly improves the chance of identifying suitable conditions for crystallization. It is also well known that homologous proteins from different sources cannot be easily crystallized using the same technique and/or conditions and may result in different crystal forms. See, for example, Jan Drenth (PTO form 891, reference U). Therefore, only the AR-LBD/dihydroxytestosterone complex crystal is enabled in the instant application.

f) The skill of those in the art of crystallography is high, however the science of determining protein structure and obtaining crystals is one encompassing many variables.

h) The claims are broad because they are drawn to an AR-LBD/ligand complex encompassing **any** ligand. The skilled practitioner would first turn to the instant specification for guidance to practice methods of generating the various crystals. However, the instant specification does not provide specific guidance to practice all of these embodiments. The specification is only enabled for an AR-LBD/dihydroxytestosterone complex crystal. As such, the skilled practitioner would turn to the prior art for such guidance. However the prior art shows that crystallography is uncertain and does not teach how to form a crystal of AR-LBD complexed with **any** ligand.

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For the reasons set forth above it would require undue experimentation for one of skill in the art to practice the claimed invention therefore the claims are not enabled.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

MARJORIE MORAN
PATENT EXAMINER

Marjorie A. Moran

October 24, 2003

Lori A. Clow, Ph.D.

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Lori A. Clow